



OncoSTRAT&GO

THE ONLY MOLECULAR PROFILING
SOLUTION COMBINING LIQUID AND
SOLID BIOPSIES

Recommended for the following metastatic solid tumors in adults:

HR+, HER2+ AND TRIPLE-NEGATIVE BREAST CANCER •
COLORECTAL CANCER • NON-SMALL CELL LUNG CANCER
• OVARIAN CANCER • PANCREATIC CANCER • CANCER OF
UNKNOWN PRIMARY (CUP)



SCREENING MORE THAN THE USUAL SUSPECTS

**A unique powerful combination for
decision-making**



Why combining liquid and solid biopsies?



THERE ARE TWO MAIN REASONS WHY THE COMBINATION OF SOLID AND LIQUID BIOSPIES IS MEANINGFUL IN CLINICAL PRACTICE

1. To decipher tumor spatial heterogeneity (presence of different mutations between the primary tumor and the metastases, as well as between the metastases). This is particularly important in stage IV patients harboring a cancer type with targeted therapies available, in order to identify resistant mutations that may not be present in the solid biopsy analysed. These mutations can be detected in the circulating tumor DNA (ctDNA) (isolated from blood).
2. To identify germline gene alterations leading to a BRCAness phenotype that are very challenging to detect in FFPE samples. These alterations can be easier identified in DNA from PBMCs (peripheral blood mononuclear cells) (isolated from blood).

OncoSTRAT&GO combines the analysis of a solid biopsy sample (from the primary tumor or a metastasis) and the analysis of a liquid biopsy (blood sample).

ctDNA

→ In 86% of metastatic patients, solid and liquid biopsies provide **different information on genetic alterations** (Finzel A. et al 2018)



RECOMMENDED FOR :

- The following stage IV solid tumors in adults:
- Non-small cell lung cancer
 - Breast cancer (HR+ and HER2+)
 - Colorectal cancer
 - Cancer of unknown primary

DNA of PBMCs

→ Inherited exon deletions/duplications leading to BRCAness phenotype are difficult to detect in FFPE biopsies (DNA degraded)



RECOMMENDED FOR :

- The following stage IV solid tumors in adults:
- Breast cancer (TNBC)
 - Ovarian cancer
 - Pancreatic cancer

OncoSTRAT&GO, the most complete solution integrating the analysis of solid and liquid biopsies



NEXT-GENERATION SEQUENCING

Solid biopsy



NEW

PANEL OF 313 GENES

ABL1	BCOR	CTNND1	FGFR2	KEAP1	NF1	PRKDC	RUNX1	TET2
ACVR1	BIRC2	CUL1	FGFR3	KIT	NF2	PSIP1	RUNX1T1	TGFBR2
ACVR1B	BIRC3	CUL3	FGFR4	KNSTRN	NFE2L2	PMS2	RXRA	TGIF1
ACVR2A	BRAF	CYP2C19	FLCN	KRAS	NKX2-1	PTCH1	SCAF4	THRAP3
AJUBA	BRCA1	CYP2D6	FLT1	KMT2A	NKX2-8	PTEN	SETBP1	TLR4
AKT1	BRCA2	DACH1	FLT3	KMT2B	NOTCH1	PTMA	SETD2	TMSB4X
AKT2	BRD7	DCUN1D1	FLT4	KMT2C	NOTCH2	PTPDC1	SF1	TNFAIP3
AKT3	BTG2	DDR2	FOXA1	KMT2D	NOTCH3	PTPDC1	SF3B1	TOP1
ALB	BTK	DICER1	FOXA2	LYN	NPM1	PTPN11	SIN3A	TOP2A
ALK	CARD11	DNMT3A	FOXQ1	MAGOH	NRAS	PTPRC	SLX4	TP53
AMER1	CASP8	DPYD	GAS6-AS1	MAP2K1	NSD1	PTPRD	SMAD2	TPMT
APC	CBL	EEF2	GATA1	MAP2K2	NTRK1	RAC1	SMAD4	TRAF3
APEX1	CCND1	EGFR	GATA2	MAP2K4	NTRK2	RAD21	SMARCA1	TSC1
APLN	CCND2	ELF3	GATA3	MAP3K1	NTRK3	RAD50	SMARCA4	TSC2
APOB	CCND3	EP300	GATA6	MAP3K4	NUP133	RAD51	SMARCB1	TSHR
AR	CCNE1	EPHA2	GNA11	MAPK1	NUP93	RAD51B	SMC1A	TXNIP
ARAF	CD44	EPHA3	GNAG	MDM2	PALB2	RAD51C	SMC3	U2AF1
ARHGAP35	CD70	EPHA5	GNAS	MDM4	PAX5	RAD51D	SMO	UGT1A1
ARID1A	CD79B	ERBB2	H3F3A	MECOM	PBRM1	RAF1	SOS1	UNCX
ARID2	CDH1	ERBB3	H3F3C	MED12	PD-1	RARA	SOX17	USP9X
ARID5B	CHD3	ERBB4	HGF	MEN1	PDGFRA	RASA1	SOX2	VHL
ATF7IP	CHD8	ERCC2	HIST1H3B	MET	PDGFRB	RB1	SOX9	WHSC1
ATM	CDK12	ESR1	HNF1A	MGA	PD-L1	RBM10	SPOP	WT1
ATP11B	CDK2	EZH2	HRAS	MLH1	PD-L2	RET	SPTA1	XPO1
ATR	CDK4	FANCA	IDH1	MPL	PIK3CA	RFC1	SPTAN1	ZFXH3
ATRX	CDK6	FANCC	IDH2	MRE11A	PIK3CB	RHEB	SRC	
ATXN3	CDKN2A	FANCD2	IGF1R	MSH2	PIK3CG	RHOA	SRSF2	
AURKA	CDKN2B	FANCE	IL6	MSH3	PIK3R1	RHOB	STAG2	
AXIN1	CEBPA	FANCF	IL6ST	MSH6	PIK3R2	RICTOR	STAT3	
AXIN2	CHD4	FANCI	IL7R	MTOR	PIM1	RNF43	STK11	
B2M	CHEK2	FANCL	INSR	MUC6	POLD1	ROS1	TAF1	
BAP1	COL5A1	FAS	JAK1	MYC	POLE	RPS6KA3	TBL1XR1	
BCL2	CREBBP	FAT1	JAK2	MYCL	PPP2R1A	RPS6KB1	TBX3	
BCL2L1	CSF1R	FBXW7	JAK3	MYD88	PPP6C	RPTOR	TCEB1	
BCL2L11	CSNK2A1	FGF3	KDM6A	MYO18A	PRKAR1A	RQCD1	TCF12	
BCL9	CTNNB1	FGFR1	KDR	NCOR1	PRKCI	RRAS2	TCF7L2	

FOR NON-SMALL CELL LUNG, BREAST (HR+, HER2+ AND TRIPLE-NEGATIVE), COLORECTAL, OVARIAN AND PANCREATIC CANCERS, AND CANCER OF UNKNOWN PRIMARY:

NGS:

313-gene panel for predicting patient response to:

- Targeted therapies (i.e. PARP inhibitors, EGFR TKIs, hormonal therapy)
- Immunotherapy

It includes **LOH**, **TMB** and **MSI** determination, important for immunotherapy response prediction.

Immunohistochemistry (IHC):

Protein expression analysis for predicting patient response to chemotherapies, immunotherapy and targeted therapies.

Additional tests:

Unusual splicing, gene fusions and promoter methylation for predicting patient response to targeted therapies.

NEW

KEY CHANGES IN THE NEW SOLID BIOPSY ANALYSIS

- **Twice as many genes sequenced (vs previous version)**
313 instead of 150 genes, leading to a more precise TMB calculation
- **Microsatellite instability (MSI)**
Broad coverage beyond the usual markers
- **Loss of heterozygosity (LOH)**
More SNP regions covered for determining LOH with a higher accuracy
- **Fusion panel**
Detection of fusion events involving ALK, ROS1, RET or NTRK1/2/3

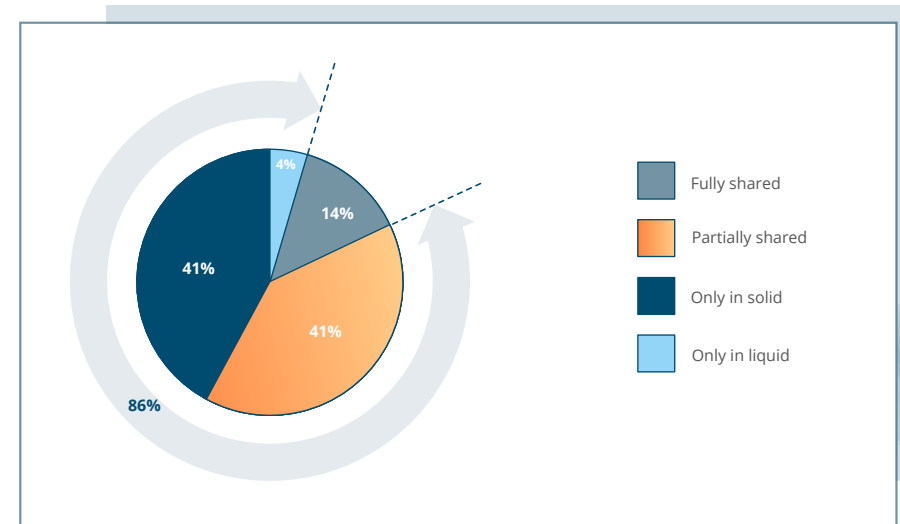


1. THE ADDED VALUE OF ctDNA: Deciphering tumor spatial heterogeneity

ctDNA profiling should be added to the analysis of solid biopsies in clinical routine for metastatic cancer types with targeted therapies available, in order to provide the most comprehensive characterization of the heterogeneity of the patient's tumor ^(Finzel A. et al 2018).

IN 86% OF THE PATIENTS, SOLID AND LIQUID BIOPSIES PROVIDE DIFFERENT INFORMATION ON GENETIC ALTERATIONS

Retrospective study evaluating 351 patients with stage IV solid tumors whose tissue and blood samples were tested using the OncoSTRAT&GO™ profiling solution and who had failed at least one line of therapy before undergoing molecular profiling ^(Finzel A. et al 2018).



Patient distribution according to discrepancy between solid and liquid biopsies.
Fully shared: Patients with the same variants detected in solid and liquid biopsies
Partially shared: Patients with variants detected only in the solid or only in the liquid biopsy and with variants detected in both biopsies
Only in solid: Patients with variants detected only in the solid biopsy
Only in liquid: Patients with variants detected only in the liquid biopsy



Liquid biopsy



WHY TO ADD ctDNA PROFILING TO SOLID BIOPSY ANALYSIS?

- To decipher the heterogeneity between the primary tumor and its related metastases, as well as between the different metastatic sites
- To identify drug-resistance mutations that would be responsible of patient's relapse

ONCOSTRAT&GO IS THE ONLY SOLUTION COMBINING LIQUID AND SOLID BIOPSIES. IT IS RECOMMENDED FOR THE FOLLOWING STAGE IV CANCERS:



Non-small cell lung cancer



HR+ and HER+ breast cancer



Colorectal cancer



Cancer of unknown primary

ANALYSIS OF CIRCULATING TUMOR DNA (ctDNA)

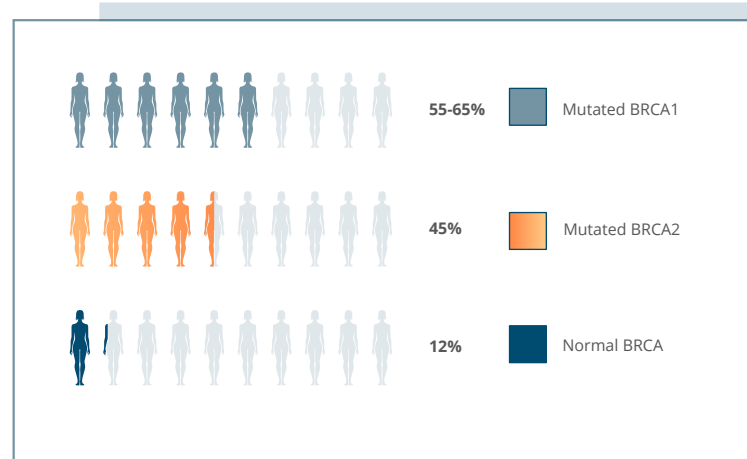
40-gene panel for predicting patient response to immunotherapy and targeted therapies.

AKT1	CKIT	ERRB2	FGFR2	GNAS	JAK3	MTOR	PTEN
ALK	CMET	ESR1	FGFR3	HRAS	KRAS	NPM1	RAF1
AR	CTNNB1	EZH2	FOXL2	IDH1	MAP2K1	NRAS	RET
BRAF	DDR2	FBXW7	GNA11	IDH2	MAP2K2	PDGFRA	ROS1
BTK	EGFR	FGFR1	GNAQ	JAK2	MPL	PIK3CA	TP53



2. THE ADDED VALUE OF DNA FROM PMBCs: Identification of germline gene alterations leading to a BRCAness phenotype

BRCA MUTATIONAL STATUS AND CANCER DEVELOPMENT

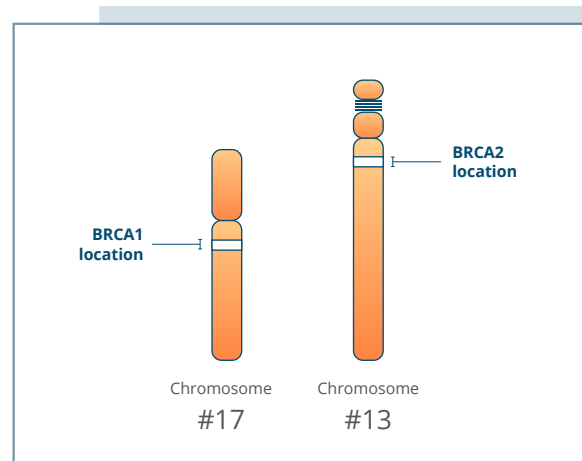


Germline mutations in BRCA1 and BRCA2 have been proven to portend an increased lifetime risk of breast, ovarian and pancreatic cancers in the individuals who carry them.

Of note, about 12% of women in the general population will develop breast cancer sometime during their lives, while about 55-65% of women who inherit a harmful BRCA1 mutation and about 45% of women who inherit a harmful BRCA2 mutation will develop breast cancer by the age of 70.

Chances of developing breast cancer by age 70

<https://www.cancer.gov/research/progress/discovery/brca-cancer-risk-infographic>



Location of BRCA1 & BRCA2

BRCA MUTATIONAL STATUS AND RESPONSE TO PARP INHIBITORS

Tumors with mutations in BRCA1/2 or in other genes that when altered lead to homologous recombination deficiency (BRCAness phenotype) are particularly sensitive to PARP inhibitors.

In fact, PARP inhibitors have been approved by the FDA for the treatment of breast and ovarian cancers with germline mutations in the BRCA1 or BRCA2 gene.

LIMITATIONS OF FFPE SAMPLES



About 5-10% of BRCA1/2 mutations are exon deletions/duplications, very difficult to detect in FFPE samples. As these alterations are germline, they can be identified in normal DNA from PMBCs.

WHY TO ADD PROFILING OF DNA FROM PMBCs TO SOLID BIOPSY ANALYSIS?

→ To identify patients sensitive to PARP inhibitors harboring BRCA1/2 alterations difficult to detect in FFPE samples (or in ctDNA)

ONCOSTRAT&GO IS THE ONLY SOLUTION COMBINING LIQUID AND SOLID BIOPSIES. IT IS RECOMMENDED FOR THE FOLLOWING STAGE IV CANCERS:



Triple-negative breast cancer



Pancreatic cancer



Ovarian cancer

ANALYSIS OF DNA FROM PMBCS

Panel for detecting germline exon deletions/duplications, which are very challenging to detect in solid biopsies (as well as in ctDNA). In addition to BRCA1/2, we also test other genes involved in the BRCAness phenotype:

APC	BRCA1	CDKN2A	MLH1	MSH6	PALB2	POLE	RAD51D
ATM	BRCA2	CHEK2	MRE11A	MUTYH	PIK3CA	PTEN	SCG5 (dup only)
BAP1	BRIP1	EPCAM	MSH2	NBN	PMS2	RAD50	SMAD4
BARD1	CDH1	GREM1	MSH3	NTHL1	POLD1	RAD51C	STK11



KEY CHANGES IN THE NEW LIQUID BIOPSY ANALYSIS

→ New BRCAness panel

To determine response to PARP inhibitors in a broader population of patients

→ Adapted technology

From normal DNA extracted from blood samples, using a technology that enables the detection of exon deletions/duplications with high accuracy

About OncoDNA solutions

We use a combination of the most relevant molecular technologies to support oncologists in their decisions for patient treatment.

Our innovative approach is to combine next-generation sequencing (NGS) with immunohistochemistry (IHC) and additional techniques. This gives a comprehensive view of the tumor profile at the DNA, RNA and protein levels and can help identify more therapeutic options for the patient. Moreover, in 2016 we included liquid biopsy analyses in our solution portfolio, either in combination with solid biopsies or as standalone.

We use a combination of the most relevant molecular technologies to support oncologists in their decisions about patient treatment

SOLID BIOPSY:



COST-EFFECTIVE SOLUTION COMBINING DNA, RNA AND PROTEIN ANALYSIS OF A TISSUE SAMPLE

OncoDEEP analyses solid biopsies by combining next-generation sequencing (313 genes), IHCs to study protein expression and additional tests. This complete tumor profiling allows to predict patient response to approved or experimental targeted drugs, immunotherapies and chemotherapies.

The NGS panel is accurately designed according to oncologists' needs in their current practice. Importantly, it also includes an accurate determination of MSI, TMB and LOH. The NGS panel is regularly updated based on new findings reported in the literature in order to provide patients with the most cost-effective solution.

MATERIAL

- 1 block or 25 slides (5 µm on SuperFrost Plus)

RECOMMENDED FOR:

- All solid tumors (stage III or IV) in adults
- Glioblastoma in children

SOLID AND LIQUID BIOPSIES:



THE COMPLETE SOLUTION INTEGRATING THE ANALYSIS OF SOLID AND LIQUID BIOPSIES

OncoSTRAT&GO is an integrated approach that combines the analyses of a solid biopsy (by next-generation sequencing (313 genes), IHCs and additional tests) with the analysis of a blood biopsy. The blood profiling focuses either on the circulating tumor DNA (for deciphering tumor heterogeneity) or in DNA from blood cells (for studying specific germline gene alterations related to BRCAness phenotype that are challenging to detect in FFPE samples).

OncoSTRAT&GO establishes a complete genetic profile of the tumor, which can be used to identify sensitivity or resistance to targeted therapies, chemotherapies and immunotherapies.

MATERIAL

- 1 blood sample (1x10 ml Streck tube or 1x10 ml EDTA tube)
- 1 block or 25 slides (5 µm on SuperFrost Plus)

RECOMMENDED FOR:

- The following stage IV solid tumors in adults:
- Non-small cell lung cancer
 - HR+, HER2+ and triple-negative breast cancer
 - Colorectal cancer
 - CUP
 - Ovarian cancer
 - Pancreatic cancer

NO SOLID BIOPSY:



CANCER-SPECIFIC SOLUTION FROM A LIQUID BIOPSY SAMPLE

OncoSELECT is a fast and minimally invasive analysis of circulating tumor DNA from a blood sample.

It is the perfect solution to identify therapeutic options for cancer patients not able to have their tumor biopsied or whose biopsy is too old. It can be used as a tool to detect treatment resistance to targeted therapies (before first-line to check the heterogeneity of the disease, or during/after treatment to check for acquired resistance mutations), as well as for monitoring cancer progression.

MATERIAL

- 2 blood samples (2x10 ml Streck tubes)

RECOMMENDED FOR:

The following metastatic solid tumors in adults:

- Non-small cell lung cancer
- Breast cancer HR+ or HER2+
- Colorectal cancer

MONITORING RESPONSE:



OncoDNA can provide also a solution for personalized monitoring.

Do not hesitate to request more information or our support at sales@oncodna.com



OncoSTRAT&GO results in an integrated theranostic report

1 MEDICAL INFORMATION

- High definition image of the tumor sample
- Clinical form with patient clinical data
- Cancer type and stage

2 NEXT-GENERATION SEQUENCING

- Complete list of variants and their biological and therapeutical impact
- List of genes sequenced
- MSI (microsatellite instability)
- TMB (tumor mutational burden)
- Alphalist: Biomarkers associated with FDA and/or EMA approved drugs with pharmacogenomic information on their labels as well as variants associated with clinical resistance or sensitivity for FDA/EMA approved drugs

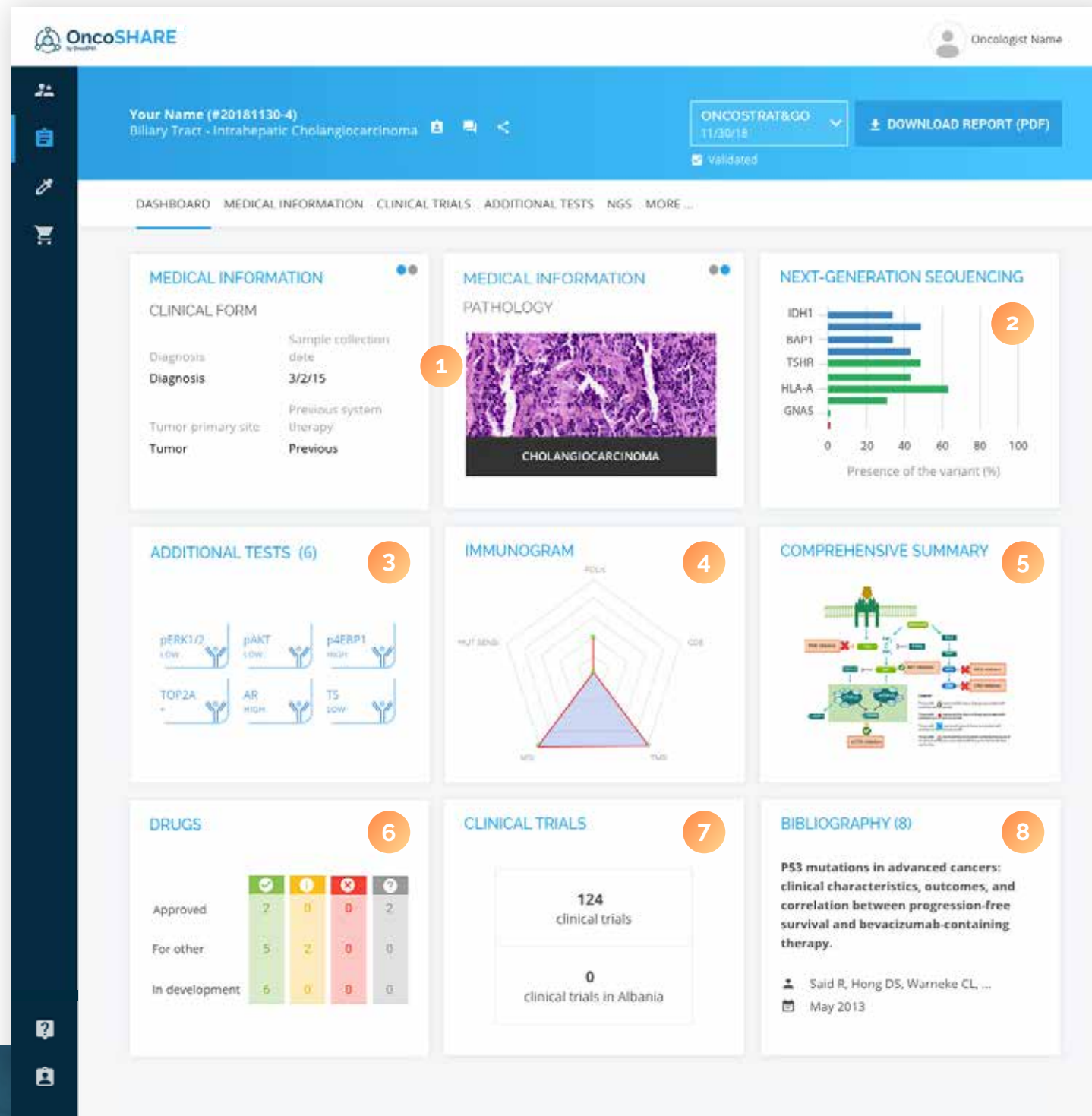
3 ADDITIONAL TESTS

- Immunohistochemistry (for chemotherapy, targeted therapy or immunotherapy)
- Unusual splicing and methylation
- Translocations or fusions

4 IMMUNOGRAM

The immunogram shows the potential response of each patient to immunotherapy. It is created from (1) the percentage of PD-L1 positive tumor cells, (2) the percentage of infiltrated CD8+ T cells, (3) the level of tumor mutational burden, (4) the microsatellite stability status of the tumor (5) the presence of mutations associated with either sensitivity or resistance to immunotherapy.

The larger the area, the better the patient should respond to immunotherapy.



5 COMPREHENSIVE SUMMARY

- List of treatment classes associated with clinical benefit or not
- Simplified molecular pathway(s)

6 DRUGS

- List of treatments associated with:
 - Potential clinical benefit
 - Potential lack of clinical benefit
 - Undetermined clinical benefit
 - Toxicity
- Tradenames, therapeutic classes, official indications
- Approval status for the type of cancer and for other indications
- Drugs in development

7 CLINICAL TRIALS

List of all clinical trials associated with certain features of the molecular profile of the patient.

8 BIBLIOGRAPHY

List of all publications and links related to the patient's molecular profile used in the report.



How to order an OncoSTRAT&GO test?

1 LOGIN TO **OncoSHARE** by OncoDNA

OncoSHARE: An easy way to access & order your tests and receive the personalised report on treatment recommendations

When you join **OncoSHARE**, you become a member of an active network gathering together more than 13 000 patients and oncologists.

Regardless of whether information concerns patient health or payment, we take every precaution to ensure your security. OncoSHARE is used by oncologists to order our solutions, to display interactive analysis reports and to connect health care professionals to each other and to our team of experts.

In a simple, interactive manner, **OncoSHARE** will guide you in your selection of the most appropriate treatment options based on the unique signature of your patient's tumor.



www.oncoshare.com

2 ORDERING THE ONCOSTRAT&GO SOLUTION

- 2.1. Proceed to payment (credit card or wire transfer)
- 2.2. We ship you the corresponding sample collection kit

3 COLLECT THE SAMPLE

Collect the biopsy and send the kit back to OncoDNA. Please print your own prepaid airway bill generated online at <https://delivery.oncodna.com>.

4 SAMPLE ANALYSIS

On arrival at the OncoDNA facilities, the sample quality is checked and the sample recorded in our tracking system for further analysis.

5 YOUR REPORT READY ON ONCOSHARE

After interpretation by our experts, the results are published in an interactive report that is made available in your OncoSHARE account.

6 WE SUPPORT YOU

Support is available at all times, for patients through our Patient Care department (infos@oncodna.com) and for oncologists via our scientific team (molecular@oncodna.com).



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by OncoDNA

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SCREENING MORE THAN THE USUAL SUSPECTS

A unique powerful combination for decision-making

REFERENCES :

• *Finzel A. et al The combined analysis of solid and liquid biopsies provides additional clinical information to improve patient care J Cancer Metastasis Treat 2018;4:21*